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APPENDICES

APPENDIX I

Effect of temperature on reaction rates

Temperature is important in pharmaceutical stability for both practical and theoretical reasons. Experrimentally, the reaction rate constant is observed to have and exponential dependence on temperature :

$$K = Ae^{-Ea/RT} \quad\text{.......................(1)}$$

The relationship is called the Arrhenius equation. This equation can be written in equivalent form as follows :

$$\ln k = \ln A - Ea/R.1/T \quad\text{................(2)}$$

where k is the rate constant, A is the frequency factor, Ea is the activation energy or heat of activation (kcal/mol), R is the gas constant (1.987 cal/mole/degree), T is the absolute temperature (degree Kelvin = °C + 273)

A plot of ln k as a function of reciprocal temperature will give a straight line plot of an intercept ln k and slope -(Ea/R). Therefore, if values of k are available at elevated temperatures, it may be possible to estimate the shelf-life at room temperature.

Estimation of rate constant at room temperture (25°C) and 8°C

Form Arrhenius equation, $\ln k_{25}$ and $\ln k_8$ were calculated by replacing T with 1/273+25 and 1/273+8, respectively. The interval of $\ln k_{25}$ and $\ln k_8$ was calculated by statistical technique. The k_{25}, k_8 and the interval of them were found by taking off the natural logarithm.

Calculation of shelf-life

In this experiment, the shelf-life at room temperature was 25°C. The shelf-life ($t_{90\%}$) that the concentration drops from 100 % to 90 % labelled amount was calculated from the first order degradation as following :

$$\ln C_t = \ln C_0 - kt \ldots (3)$$

$$\ln C_t - \ln C_0 = -kt \ldots (4)$$

$$\ln 90 - \ln 100 = -kt \ldots (5)$$

$$\ln 90/100 = -kt \ldots (6)$$

$$t_{100-90} = 0.1054/k \ldots (7)$$

The shelf-life according to the 90-100 % LA was calculated by replacing k with k_{25}, k_8 and the interval of them.

On the other hand, The content of chloramphenicol eye drops BPC 1973 and BP 1993 was limited between 90-110% labelled amount, the shelf-life according to BPC 1973 and BP 1993 will be the duration that the concentration drops from 110% to 90% labelled amount. The equation was

$$t_{110-90} = 0.2007/k \ldots (8)$$

The shelf-life according to BP 1993 were calculated by the same method.

APPENDIX II

The Code of Federal Regulation directs that if the five corrected mean responses plotted on an arithmetic scale against dose on a logarithmic scale appear to describe a straight line, then the two following values be calculated. These values may be described as corrected ideal responses to low and high doses. They are denoted by L and H respectively, and are calculated as

$$L = \frac{3a+2b+c-e}{5}$$

$$H = \frac{3e+2d+c-a}{5}$$

L = Calculated zone diameter for the lowest concentration of the standard response line.

H = Calculated zone diameter for the highest concentration of the standard response line.

c = Average zone diameter of 36 readings of the reference point standard solution.

a, b, d, e = Corrected average values for the other standard solution, lowest to highest concentration, respectively.

These two values for L and H are plotted on the semilog graph paper and give the best straight line that can be drawn from the experimental data.

APPENDIX III

Paired t-test $\quad = \quad \dfrac{\bar{d}}{S_{\bar{d}}}$

$\alpha \quad = \quad .05$

$d \quad = \quad$ The average of different zone diameter between chloramphenicol and chloramphenicol : HP-β-CD complex

$\qquad = \quad \dfrac{\Sigma d}{n}$

$S_{\bar{d}} \quad = \quad$ Error of different values

$\qquad = \quad \sqrt{S_{d^2}/n}$

$S_{d^2} \quad = \quad$ Variance of the different values

$\qquad = \quad \dfrac{\Sigma d^2 - (\Sigma d)^2/n}{n-1}$
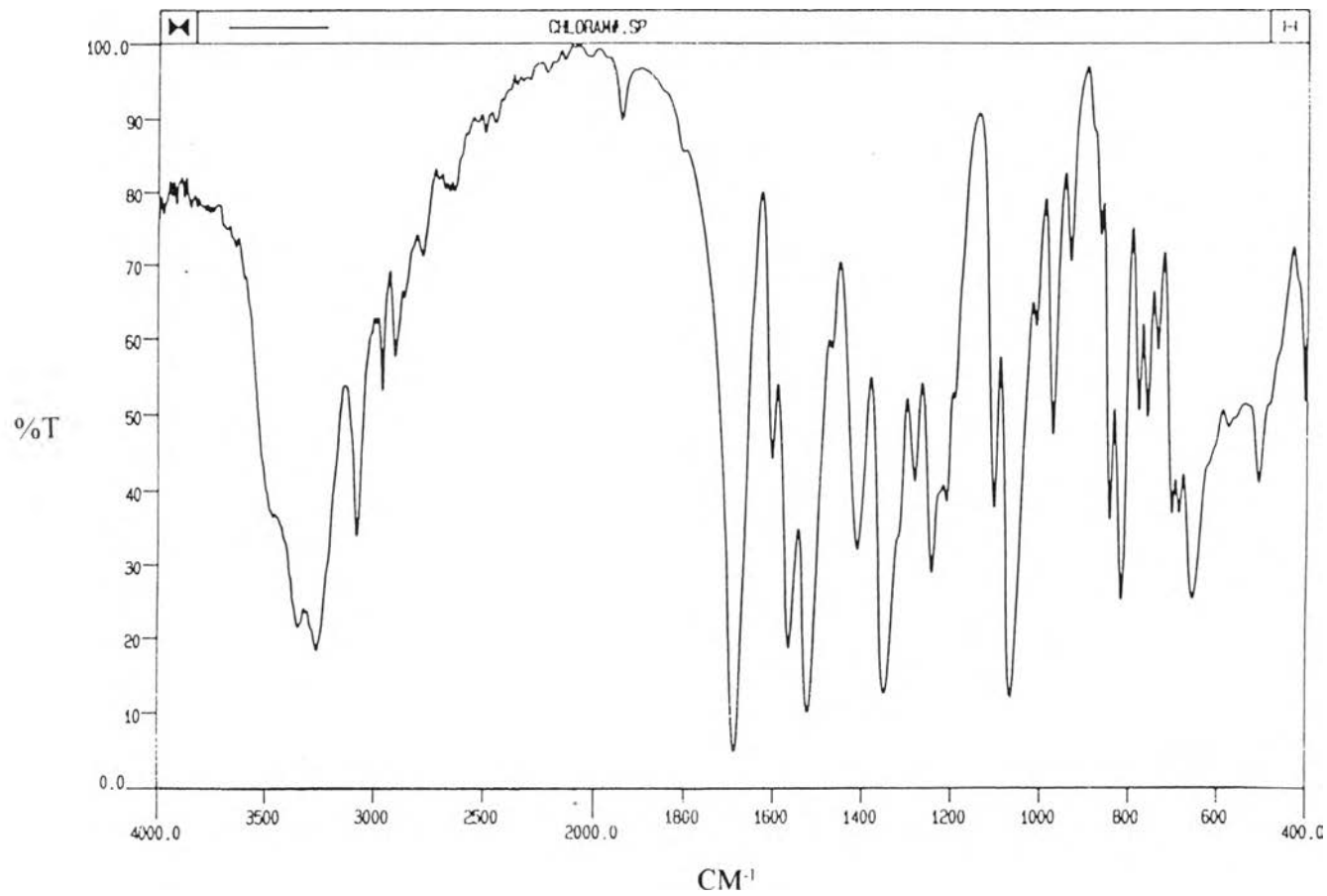
Figure 31 FTIR spectrum of chloramphenicol.
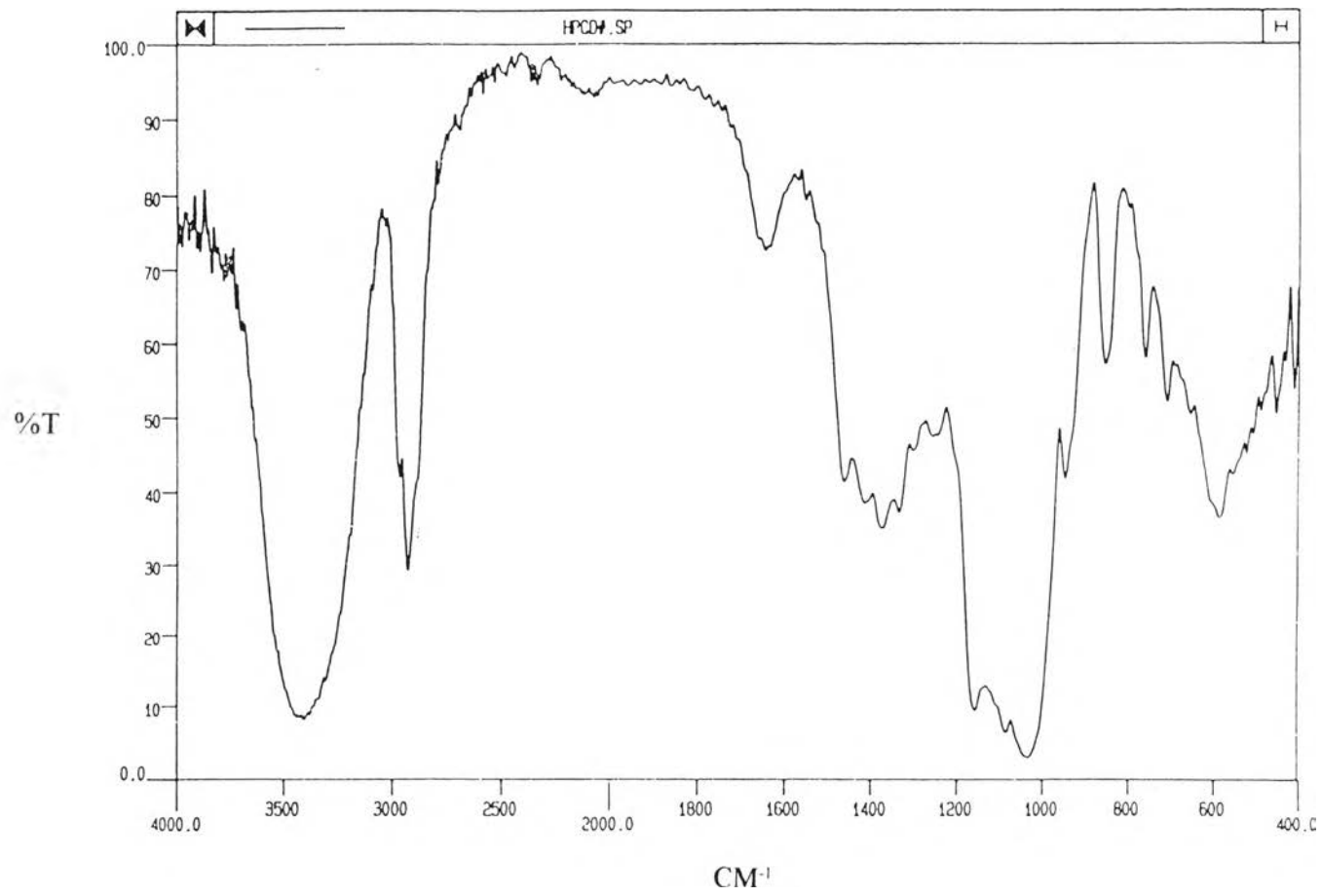
Figure 32 FTIR spectrum of 2-HP-β-CD.
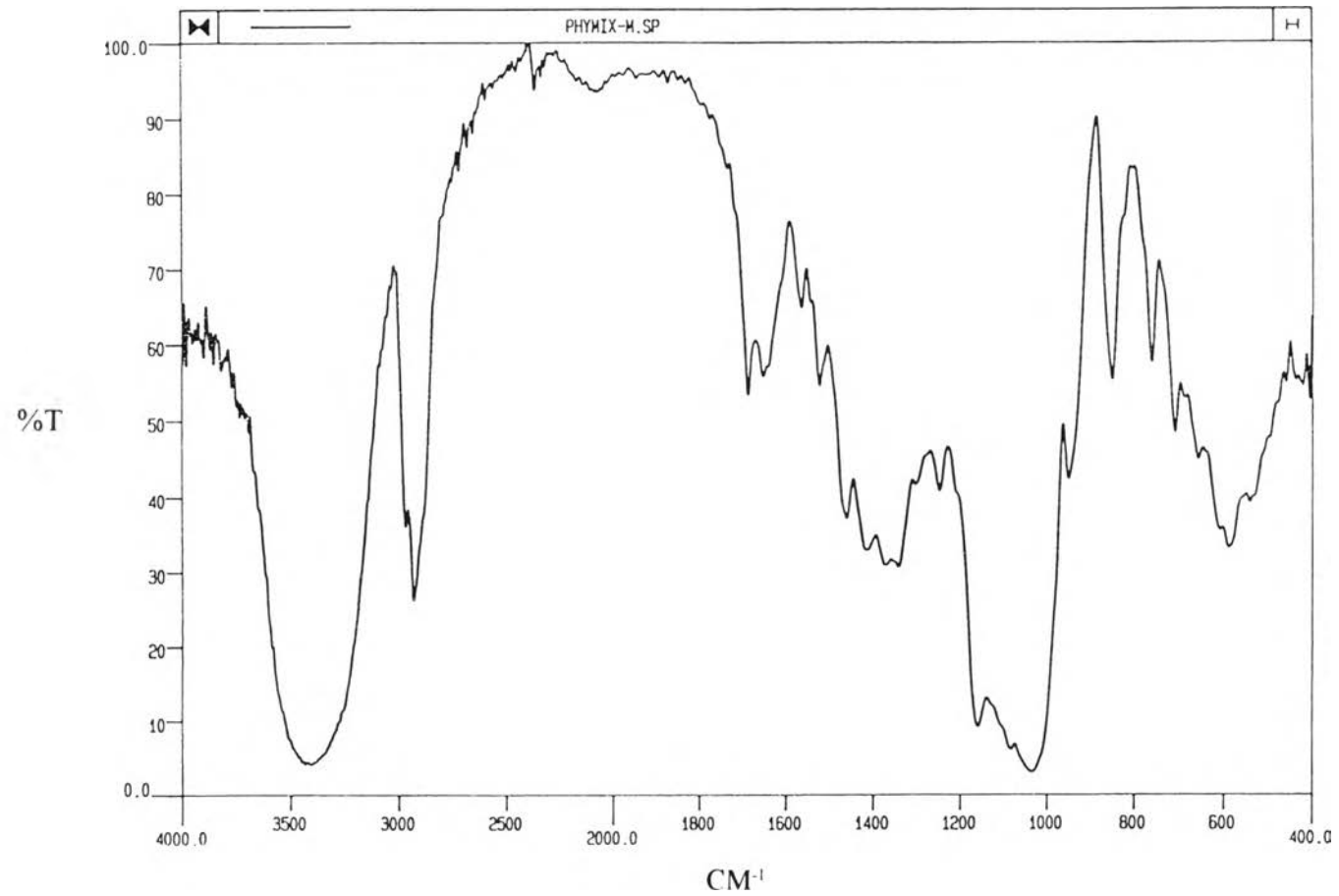
Figure 33 FTIR spectrum of physical mixture.
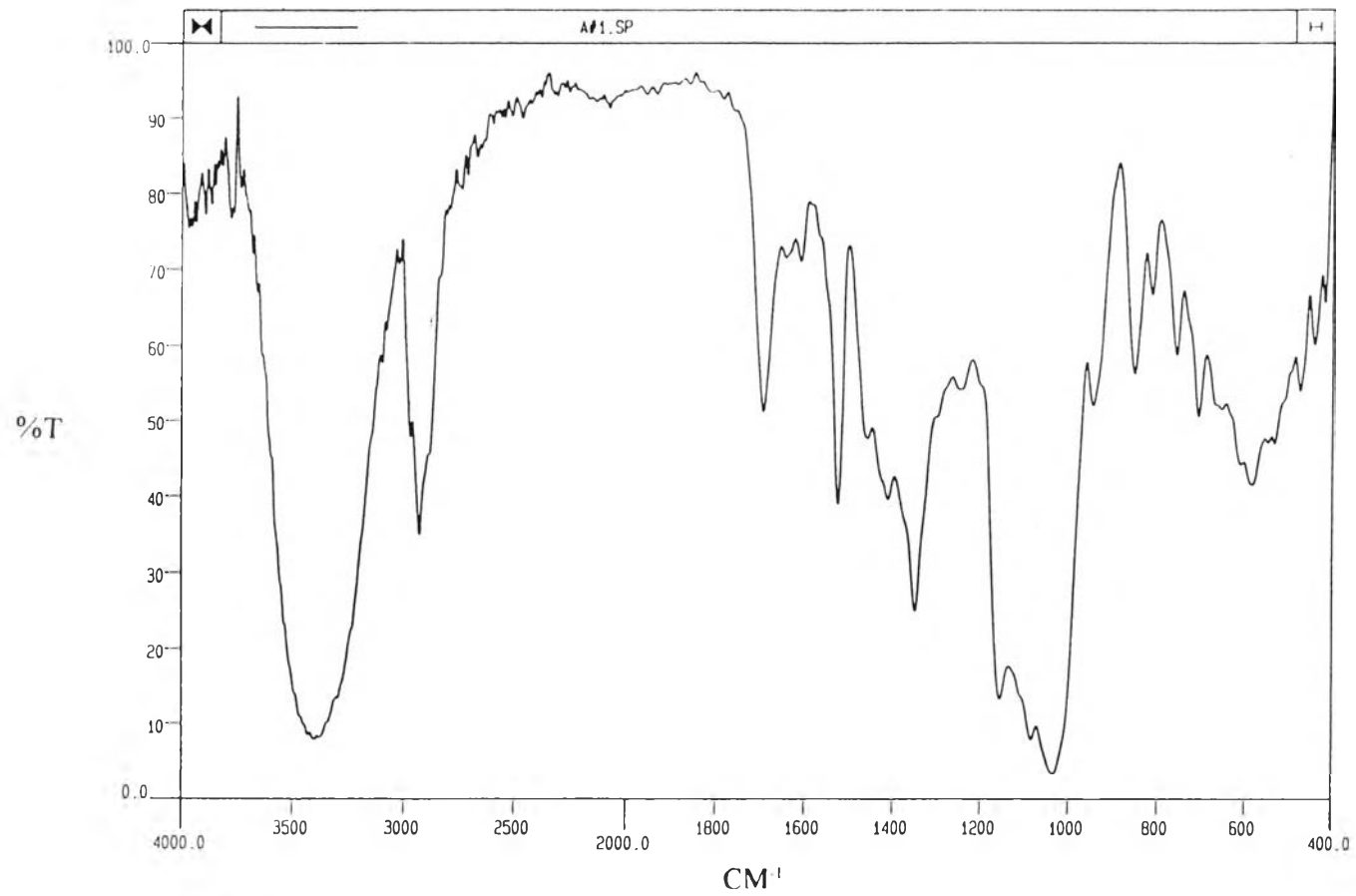
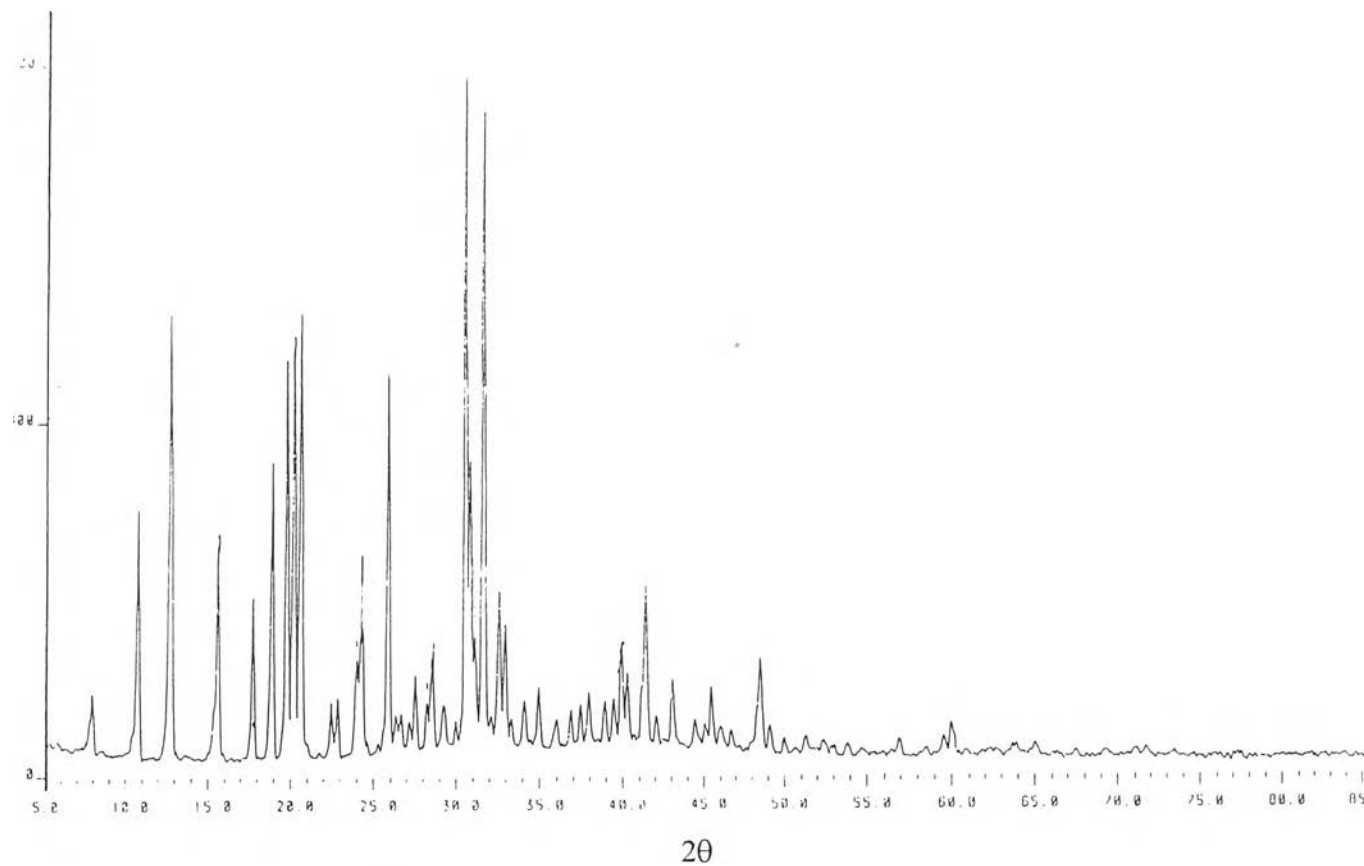Figure 34 FTIR spectrum of chloramphenicol : 2-HP-β-CD complex.

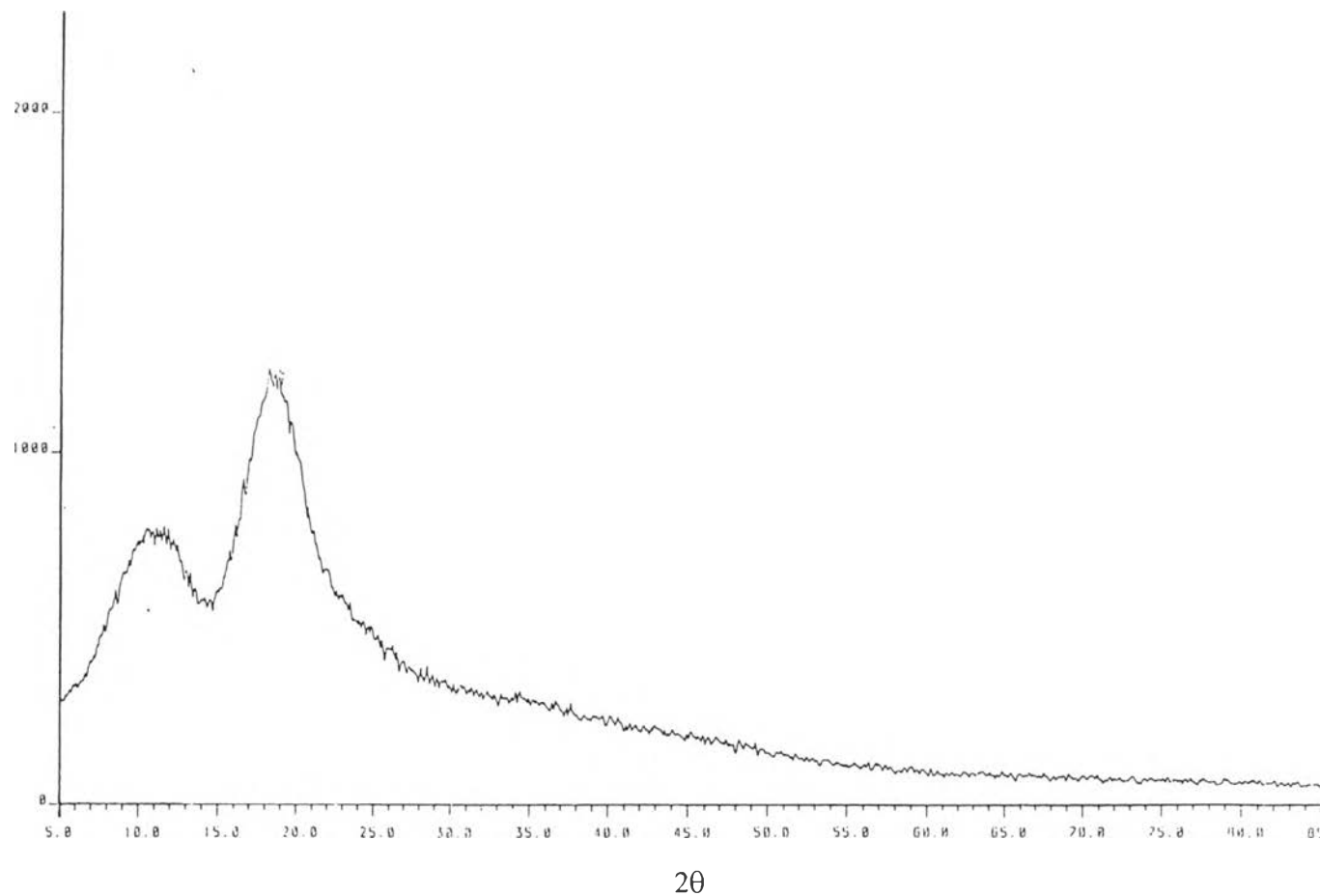Figure 35 X-ray diffraction pattern of chloramphenicol.

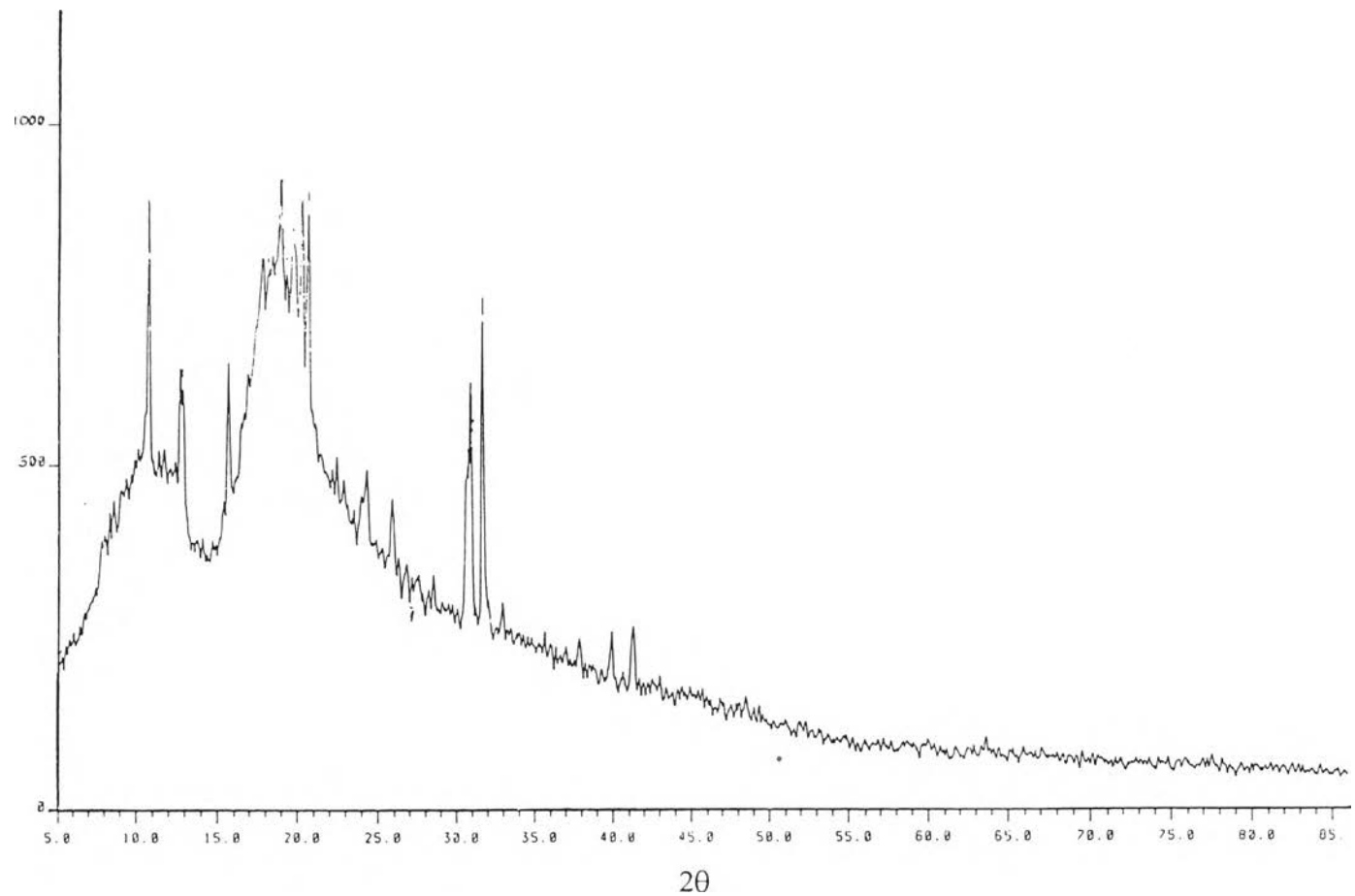Figure 36 X-ray diffraction pattern of 2-HP-β-CD.

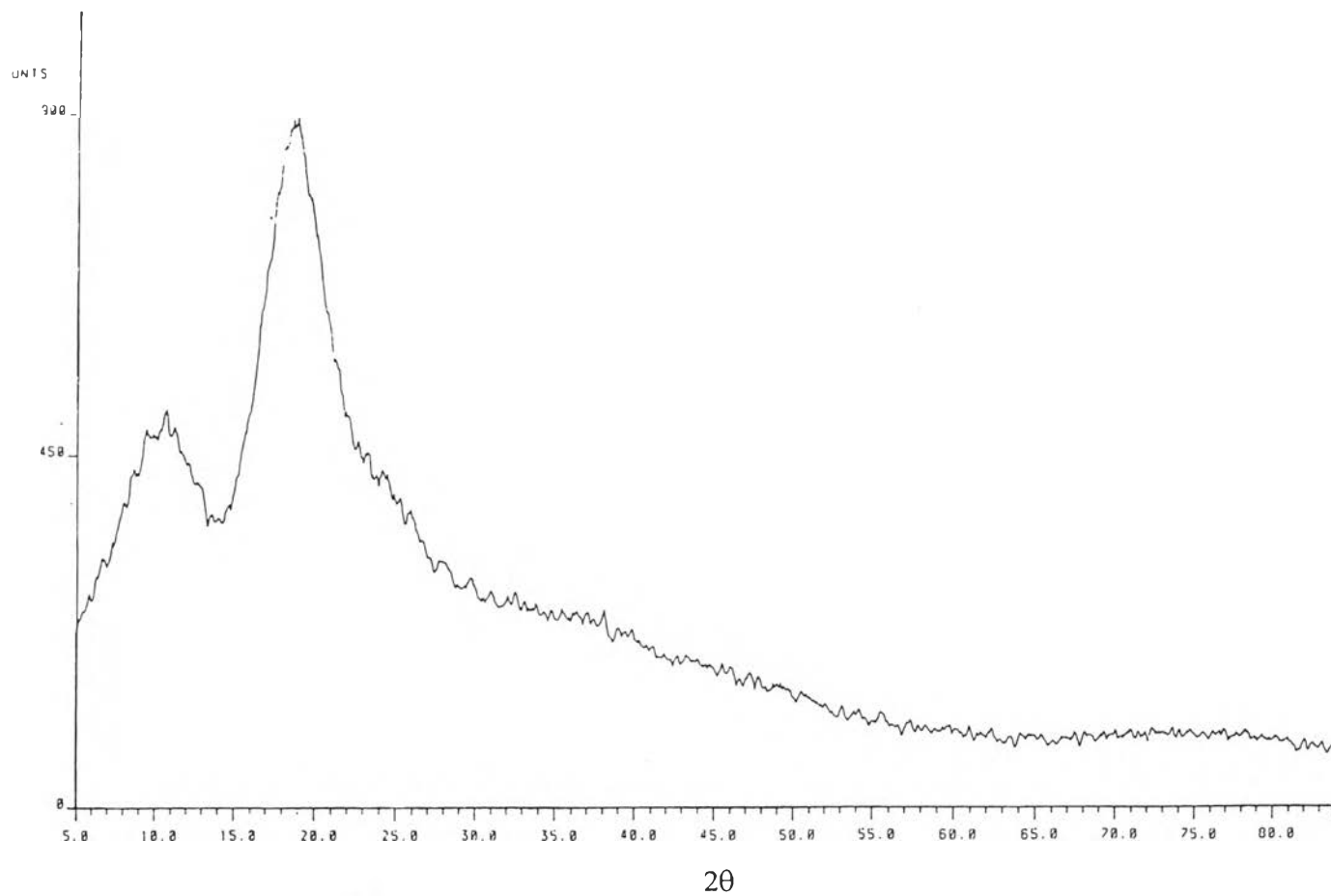Figure 37 X-ray diffraction pattern of physical mixture.

Figure 38 X-ray diffraction pattern of chloramphenicol : 2-HP-β-CD complex.

VITAE

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